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EXAMINER	
STEELE, JENNIFER A	

ART UNIT	PAPER NUMBER
1794	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,123	GOHL ET AL.	
	Examiner	Art Unit	
	JENNIFER STEELE	1794	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-21 and 24-27* is/are pending in the application.

4a) Of the above claim(s) *8-19,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 20-21, 24-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim 1, 3, 5-7, 20-21 and 24-25 rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0568045.

Claim 1 describes a permselective asymmetric hollow fiber membrane suitable for hemodialysis comprising:

- at least one hydrophobic polymer and
- at least one hydrophilic polymer
- wherein said hollow fiber membrane has a four layer structure comprising
    - a first inner separation layer in the form of a dense rather thin layer
    - a second layer in the form of a sponge structure
    - a third layer in the form of a finger structure
    - and a fourth outer layer in the form of a sponge layer having an outer surface having pores with sizes in the range of 0.5-3 micron, the number of said pores on the outer surface of the sponge layer being in the range of 10,000 to 150,000 pores per mm^2

EP '045 teaches a polysulfone hollow fiber membrane with an inner dense skin layer composed of polysulfone and a lesser amount of polyvinylpyrrolidone. A polysulfone is a hydrophobic polymer and the polyvinylpyrrolidone is a hydrophilic

polymer as taught in Applicant's own specification [0032] and [0033]. EP '045 teaches hollow fiber membranes are asymmetrical (page 10, lines 46).

EP '045 teaches dense skin layer on the inner surface of 0.1-3 micron thick for separating substances from filtrates which contains micropores having a pore diameter gradually increasing toward a core layer supporting the skin layer (page 10, lines 47). This structure where the pores gradually increase is equated with the second layer in the form of a sponge structure.

EP '045 teaches a supporting core layer of reticular texture having micropores of a 1-5 micron average pore diameter and this layer is equated with Applicants third layer of a finger structure as a finger would be reticular structure.

EP '045 teaches outer surface layer of reticular texture having micropores of a 0.1-0.5 micron average pore diameter on the outer surface, as the ranges overlap at 0.5 micron average pore diameter (page 10, lines 44-51). EP '045 shows the structure of the outer surface layer of the polysulfone-based hollow fiber membrane in Fig. 1 which shows that there is a number of pores present, however EP '045 differs and does not teach the number of pores present on the outer surface. EP '045 further teaches the process conditions can be modified to optimize the outer surface structure. EP '045 teaches a dry-jet-wet spinning process wherein extrudates pass through a gaseous atmosphere, generally air, during traveling from the outlet of the orifice to the coagulating bath which is called the "dry zone". When the "dry zone" is humidified, the moisture in air may promote microphase separation whereby hollow fiber membranes having many micropores of relatively large diameter in their outer surface can be readily

obtained. EP ‘045 presents a finding that one of ordinary skill in the art could optimize the process conditions to obtain the desired pore size and number of pores with a reasonable expectation of success.

As to claim 3, EP ‘045 differs and does not teach the property of diffusive permeability. As EP ‘045 teaches the same structure and materials as the claimed invention, it is presumed that the property of diffusive permeability is inherent to the structure of EP ‘045.

As to claim 5, EP ‘045 teaches the membrane has a composition of hydrophobic polymer of to hydrophilic polymer in the range of 90% hydrophobic and 10% hydrophilic and 60% hydrophobic and 40% hydrophilic which encompasses the claim ranges of 65-95% hydrophobic polymer and 5-35% hydrophilic polymer.

As to claim 6, EP ‘045 teaches the hydrophobic polymer is polysulfone which is equated with polysulphone.

As to claim 7, EP ‘045 teaches the hydrophilic polymer is polyvinylpyrrolidone.

As to claims 20 and 21, EP ‘045 teaches the membranes are for use for hemodialysis, hemofiltration and hemoconcentration.

As to claim 24 and 25, EP ‘045 differs and does not teach the number or density of pores on the outer surface. EP ‘045 further teaches the process conditions can be modified to optimize the outer surface structure. EP ‘045 teaches a dry-jet-wet spinning process wherein extrudates pass through a gaseous atmosphere, generally air, during traveling from the outlet of the orifice to the coagulating bath which is called the “dry zone”. When the "dry zone" is humidified, the moisture in air may promote microphase

separation whereby hollow fiber membranes having many micropores of relatively large diameter in their outer surface can be readily obtained. EP '045 presents a finding that one of ordinary skill in the art could optimize the process conditions to obtain the desired pore size and number of pores on the surface with a reasonable expectation of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claim 1, 3-7, 20-21, 24-25 rejected under 35 U.S.C. 103(a) as unpatentable over Buck (US 4,935,141) in view of EP 0568045.

Buck teaches a permeable asymmetric membrane preferably in the shape of hollow fibers (ABST). Buck teaches a three layer membrane with a dense inner layer of

thickness of less than 1 micron, a second sponge layer with a thickness of 5 micron and a third open finger like structure having a thickness of 20 to 60 micron. Buck teaches a selectively permeable asymmetric membrane in which the membrane includes a

- A first layer comprising a dense, thin skin layer including substantially uniform pore openings (col. 2, lines 5-18). The first layer has a pore size of about 80 angstroms (0.008 micron). Buck teaches publication EP-A-O 168 783 which has a sponge like structure throughout its entire thickness and the inner membrane pore size of about 150 angstroms (0.015 micron). The pores then increase to the outer side (col. 4, lines 37-49).
- A second intermediate layer in contact with the first layer in the form of a sponge which has a diffusive permeability which is higher than that of the first layer (col. 2, lines 5-18). .
- And a third intermediate second layer and including a finger-like structure providing mechanical stability for the membrane. The third layer includes the finger-like structure and is equated with Applicants fourth outer layer and the third finger structure layer (col. 2, lines 5-18).

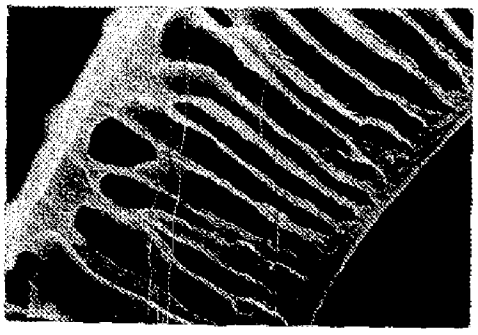
Buck shows the structure in Fig. 1b. Further, a side-by-side comparison of the photomicrographs of Buck ‘141 and the current application indicates that the prior art to Buck has the same structure as the current application.

Buck inherently has an outer layer, different from the finger-like structure and this outer layer is equated with Applicant's fourth layer. The membrane of Buck is in the form of a sponge layer and sponge layers are known to have pore sizes. Buck teaches

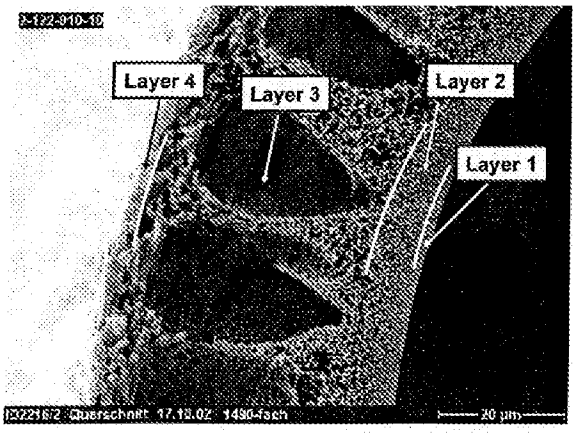
embodiments wherein the inner layer has a pore size of 0.008 to 0.015 micron and that the pore size increases towards the outer layer. The current application teaches in the specification that the inner layer has pores sizes of 5-20 nm (0.005- 0.02 micron) [0027].

As shown in the figures below, with prior art of Buck '141 on the left and the current application on the right. Buck differs and does not teach the pore size of the outer layer. However, Examiner presumes that the structure of Buck has the stated properties of an outer surface is sponge-like with a pore size of 0.5 to 3 micron and that it would have been obvious to produce a membrane with a outer layer pore size in the range of 0.5 to 3 micron based on the teaches of Buck which has the same sponge-like and finger-like structure of layers and the same inner layer pore size.

Buck is teaching an asymmetric membrane for use in hemodialysis and teaches the membrane is designed to obtain a diffusivity of urea (col. 50-68). Buck teaches the membrane structure has high diffusive permeability for low molecular weight substances, a high permeability for middle molecular weight substances and has an ultrafiltration rate which is readily adaptable to hemodialysis, hemodiafiltration and hemofiltration (col. 4, lines 1-7). It further would have been obvious to produce an outer sponge layer with the property of pore density in the range of 10,000 to 150,000 pores per mm^2.



Buck (US 4,935,141) FIG. 1b



Current Application 10/540,123 Fig. 4

As to Applicant's limitation that the outer layer has a sponge structure of a pore size that is 0.5 to 3.0 micron, Buck differs and does not teach this limitation. The reference to Kawata, EP 0568045 teaches an outer surface layer of reticular texture having micropores of a 0.1-0.5 micron average pore diameter on the outer surface, as the ranges overlap at 0.5 micron average pore diameter (page 10, lines 44-51). EP '045 is directed to an assymetrical hollow fiber membrane for use in hemadialysis filtration.

It would have been obvious to employ outer surface layer with a pore size as taught by EP '045 in the hollow fiber membrane structure of Buck motivated to produce an assymetrical membrane with the desired diffusive permeability.

As to claim 3, Buck teaches a diffusive permeability of 110 to 150 x 10^{-5} cm/sec (col. 4, lines 65-66) which is equivalent to 11 to 15 10^{-4} cm/sec and overlaps the claimed range. While citation does not explicitly state that this diffusive permeability is for urea, however Buck teaches urea clearance versus bloodflow at different ultrafiltration rates presented in Fig. 8. It is reasonable to presume that the invention of

Buck has the claimed property. When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention the examiner has basis for shifting the burden of proof to applicant as in In re Fitzgerald, 619 F.2d 67, 205 USPQ 594 (CCPA 1980). See MPEP § 2112-2112.02

As to claim 4, Buck teaches an inner layer thickness of 1 to 20 micron, a second layer thickness of 3 to 5 micron and a third layer thickness of 20 to 60 micron. As noted above, Buck does not explicitly teach a fourth layer but Buck has an outer surface layer that is included in Buck's disclosure of the third layer including a finger like structure. As such, Buck does not disclose an outer layer thickness. It would have been obvious to one of ordinary skill in the art at the time the invention was made employ an outer layer with a thickness between 1 to 10 micron motivated by Buck which teaches the same structure as shown in the figures above. As the inner layer and outer layer of the claimed invention are reasonably the same thickness, and the photomicrographs are to scale representations of the membranes, it would appear that the outer layer of Buck is in the claimed range of the Applicant's invention.

As to claim 5, Buck teaches a hydrophobic polymer between about 85-95% and a hydrophilic polymer between about 5-15% (col. 2, lines 26-32).

As to claim 6, Buck teaches the hydrophobic polymers are polyamides, polyarylsulphone, polycarbonate as disclosed in col. 2, lines 33-45).

As to claim 7, Buck teaches hydrophilic polymers such as polyvinylpryrolidone, polythyleneglycol, polypropyleneglycol, water soluble cellulosic derivative as disclosed in col. 2, lines 40-45).

As to claim 20 and 21, Buck teaches a hollow fiber membrane for use in hemodiafiltration and dialysis and filtration.

As to claims 24 and 25, Buck is teaching an asymmetric membrane for use in hemodialysis and teaches the membrane is designed to obtain a diffusivity of urea (col. 50-68). Buck teaches the membrane structure has high diffusive permeability for low molecular weight substances, a high permeability for middle molecular weight substances and has an ultrafiltration rate which is readily adaptable to hemodialysis, hemodiafiltration and hemofiltration (col. 4, lines 1-7). It further would have been obvious to produce an outer sponge layer with the property of pore density in the range of 10,000 to 150,000 pores per mm^2.

3. Claim 4 rejected under 35 U.S.C. 103(a) as obvious over EP 0568045 in view of Buck (US 4,935,141) and Maeda et al (US 5,707,522).

As to claim 4, EP '045 teaches the membrane can have a total membrane thickness of 5 to 250 micron. EP '045 teaches a first inner separation layer has a thickness of 0.1 to 3 micron thick and in the claimed range of less than 1 micron. EP '045 differs from the current application and does not teach the layer thickness of the second, third and fourth or outer layer.

Buck teaches a selectively permeable asymmetric membrane suitable for use in hemodialysis and processes for manufacturing such membranes (Title). Buck teaches the membranes are preferably formed in the shape of hollow fibers (ABST). Buck teaches a three layer membrane with a dense inner layer of thickness of less than 1 micron, a second sponge layer with a thickness of 5 micron and a third open finger like structure having a thickness of 20 to 60 micron. Buck shows the structure in Fig. 1b.

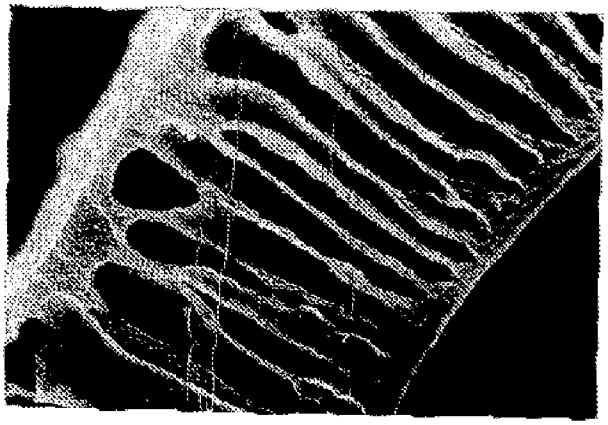


FIG. 1b

Maeda teaches a permselective membrane that is comprised of a hollow fiber asymmetric membrane having an outermost layer of a dense skin layer having a thickness of 0.05 to 5 micron and is characterized as having pore sizes of at least 0.5 micron (col. 3, lines 19-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a permselective asymmetric hollow fiber membrane with the layer thicknesses as claimed motivated to produce a membrane with the desired properties of permeability and selectivity of permeable compounds.

Response to Arguments

4. Applicant's arguments, filed 1/21/2009, with respect to the 35 USC 102/103 rejection over claims 1,3,5-7, 20-21 and 24-25 over EP '045 have been fully considered and are persuasive. The 35 USC 102/103 of claims 1, 3, 5-7, 20-21 and 24-25 has been withdrawn. Applicant's arguments with respect to claim 1, 3, 5-7, 20-21 and 24-25 have been considered but are moot in view of the new ground(s) of rejection. Applicant noted that Examiner concedes that "EP '045 differs and does not teach the number of pores present on the outer surface". Examiner states that EP '045 the micropore size and number can be optimized and therefore presents a finding that one of ordinary skill in the art could optimize the process conditions to obtain the desired pore size and number of pores. This Office Action presents a 35 USC 103(a) rejection of claims 1, 3, 5-7, 20-21 and 24-25 over EP '045. As a result the Office Action is being made nonfinal.

Applicant argues that Kawata (EP '045) does not find, teach, disclose or suggest optimizing the process conditions to obtain the desired number of pores and the Applicant's claims recite the limitation of pores per mm^2. Kawata teaches that the pore size and number of pores can result from different process conditions and this teaching is noted as a teaching that one of ordinary skill in the art could change the pore size and number of pores if so desired. Changing the pore size and number of pores to obtain a desired result would be optimizing the process to achieve a desired result.

The Applicant's claimed pore density would be derived from a pore size and a number of pores. In other words, a density property would be inherent to the structural

limitation of a number of pore present on the surface combined with the known pore size. Further as the rejection has been revised as a obviousness rejection, it would have been obvious to obtain the desired density based on Kawata that teaches one can change the size and number of pores present on the surface of the membrane.

5. Applicant argues that the Examiner failed to establish inherency in the 35 USC 102(b) rejection over claim 1 to Buck. Applicant argues that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference and that it would be so recognized by person of ordinary skill. As to the limitation of the pore size of the outer layer being 0.5 to 3 micron, Buck does not teach this limitation and as this limitation is one of structure, the previous 102/103 rejection over Buck has been withdrawn and new 35 USC 103 rejection over Buck presented in this Office Action.

However, while Buck teaches a three-layer structure and Applicant's argue the express disclosure of Buck therefore rebuts any presumptions presented by the Examiner. Examiner maintains that there is a fourth and outer layer in addition to the third finger-like structure layer described by Buck. Buck teaches that “the third layer in contact with the intermediate second layer and including a finger-like structure providing mechanical stability" (col. 2, lines 8-12). The third layer of Buck is the outer layer and it includes the finger like layer which would be two layers and would be equated with Applicant's third and fourth layers.

Applicant’s limitation of the pore density of 10,000 to 150,000 pores per mm^2 is rejected over Buck as being inherent to the structure and obvious over Buck. The pore

size of the outer layer of Buck is not disclosed. However, Buck teaches embodiments where the pore size increases from the inner layer to the outer layer and Buck teaches the same pore size of the inner layer as found in Applicant's disclosure in the specification. Further Buck teaches membranes for the same use as Applicant such as hemodialysis and teaches the same diffusive permeability. Buck teaches the pore size impacts the properties of the membrane. While it would have been obvious to select a larger pore size for the outer layer as taught by Buck, as Buck does not teach the outer surface pore size a secondary reference to Kawata is used to show that one of ordinary skill in the art could have combined the known elements from Kawata and Buck to arrive at an asymetrical membrane with the desired diffusivity properties.

6. Applicant argues that Maeda does not disclose a surface layer with pore sizes being in the range of 10,000 to 150,000 pore per mm^2 and therefore does not remedy the deficiencies of Buck. As Examiner presents in the current Office Action that the pore density would inherently be present in a sponge surface structure with a pore size as taught by EP '045 and Buck combined. Maeda is relied upon for teaching a permselective membrane that is comprised of a hollow fiber asymmetric membrane having an outermost layer of a dense skin layer having a thickness of 0.05 to 5 micron and is characterized as having pore sizes of at least 0.5 micron. One of ordinary skill in the art could have combined the known features with a reasonable expectation of success in producing an asymetrical hollow fiber membrane with the desired properties of diffusive permeability.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER STEELE whose telephone number is (571)272-7115. The examiner can normally be reached on Office Hours Mon-Fri 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald Tarazano can be reached on (571) 272-1515. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. S./
Examiner, Art Unit 1794

/Elizabeth M. Cole/
Primary Examiner, Art Unit 1794

4/6/2009